Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (ORIGINAL) Stealthy polymeric biodegradable nanospheres each comprising:

(i) a polyester-polyethylene multiblock copolymer;

(ii) optionally a polyester entangled with the multiblock copolymer to give rigidity to the nanospheres; and

(iii) optionally a pharmaceutical compound incorporated therein.

2. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 1, wherein said nanospheres comprise:

from 0.1% to 100% of the polyester-polyethylene multiblock copolymer;

from 0% to 99% of the polyester; and

from 0.1% to 20% of the pharmaceutical compound.

3. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to claim 1 ~~or 2~~, wherein the polyester-polyethylene multiblock copolymer comprises a series of polyester and polyethylene blocks which alternate so as to form a repetitive sequence.

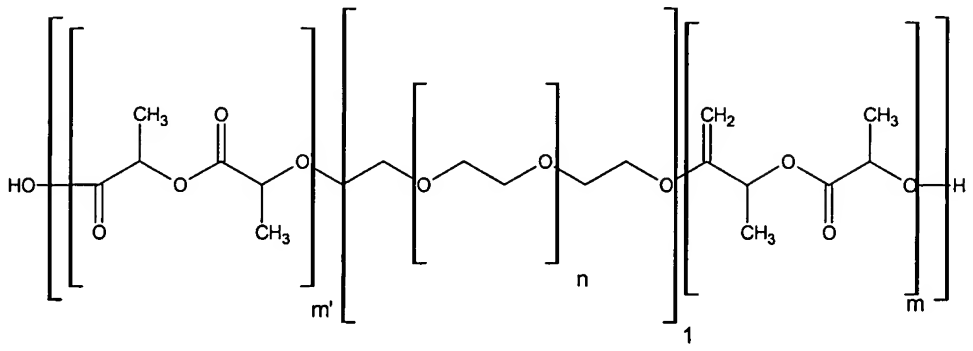
4. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 3, wherein the polyester-polyethylene multiblock copolymer is of the formula (I).

$$ABA\text{-}(c\text{-}ABA)_n\text{-}c\text{-}ABA \qquad (I)$$

wherein

- n is a number equal or greater than 2;
- ABA is a PLA-PEG-PLA triblock; and
- c is a carboxylic diacid.

5. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 4, wherein the ABA triblock is of the formula (VII):



(VII)

wherein n and m are numbers equal to or greater than 1.

6. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~claims 4 and 5~~ claim 4, wherein the carboxylic diacid is selected from the group comprising of butanedioic acid, propanedioic acid and pentanedioic acid.

7. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to claim 3, wherein the multiblock copolymer is of the formula (III):

$$ABA\text{-}B'\text{-}(ABA\text{-}B')_n\text{-}ABA \qquad (III)$$

wherein

- A is a polyester,
- B is a polyethylene;
- B' is a dicarboxylic polyethylene; and
- n is a number equal to or greater than 2.

8. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~claims~~ claim 7, wherein the polyester is selected from the group consisting of

polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), polycaprolactone (PCL), and polyhydroxy butyrate.

9. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 8 wherein the polyester is a polylactic acid (PLA).

10. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 7 wherein said polyethylene is a polyethylene oxide (PEO).

11. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 10, wherein the polyethylene oxide (PEO) is a polyethylene glycol (PEG).

12. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~any one of claims 7 to 11~~ claim 7, wherein the dicarboxylic polyethylene is selected from the group of dichloride dicarboxylic (PEG) and dibromide dicarboxylic PEG.

13. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~any one of claims 1 to 12~~ claim 1, wherein the polyester (ii) is selected from the group consisting of polylactic acid (PLA), polylactic-co-glycolic (PLGA), polycaprolactone (PCL) and their copolymers.

14. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 13, wherein the polyester (ii) is polylactic acid (PLA).

15. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~any one of claims 1 to 14~~ claim 1, wherein the pharmaceutical compound (iii) is a drug, a protein and/or a nucleic acid molecule for the prevention or treatment of various diseases and/or delivery of different types of therapeutic agents.

16. (ORIGINAL) The stealthy polymeric biodegradable nanospheres according to claim 15, wherein the therapeutic agents are selected from the group consisting of anticancer agents, immunosuppressive agents, agents for steroid therapy, anti-arrhythmic agents, antibiotics,

antiparasitics, antivirals, antifungics, gene-therapy agents, antisense molecules, orphan drugs, and vitamins.

17. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~any one of claims 1 to 16~~ claim 1, wherein the nanosphere has an average size of less than 800 nm.

18. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~claims~~ claim 17, wherein the average size is about 200 nm to 5 μm.

19. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to claim 17 ~~or 18~~, wherein the average size is about 100 nm to 10 μm.

20. (CURRENTLY AMENDED) The stealthy polymeric biodegradable nanospheres according to ~~any one of claims 1 to 19~~ claim 1, wherein the nanosphere has a zeta potential close to 0 mV.

21. (CURRENTLY AMENDED) Use of stealthy polymeric biodegradable nanospheres according to ~~any one of claims 1 to 20~~ claim 1 for the preparation of a medicament having a long term, controlled and non-toxic release of a pharmaceutical compound into a mammal.

22. (ORIGINAL) A polyester-polyethylene multiblock copolymer of formula (III):

$$ABA\text{-}B'\text{-}(ABA\text{-}B')_n\text{-}ABA \qquad (III)$$

wherein

- A is a polyester;
- B is a polyethylene;
- B' is a dicarboxylic polyethylene; and
- n is a number equal or greater than 2.

23. (ORIGINAL) The polyester-polyethylene multiblock copolymer according to claim 22, wherein the polyester is selected from the group consisting of polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), polycaprolactone (PCL), and polyhydroxy butyrate.

24. (CURRENTLY AMENDED) The polyester-polyethylene multiblock copolymer according to claim 22 ~~or 23~~, wherein the polyester consists of polylactic acid (PLA).

25. (CURRENTLY AMENDED) The polyester-polyethylene multiblock copolymer according to ~~any one of claims 22 to 24~~ claim 22, wherein the polyethylene is a polyethylene oxide (PEO).

26. (ORIGINAL) The polyester-polyethylene multiblock copolymer according to claim 25, wherein the polyethylene oxide (PEO) is a polyethylene glycol (PEG).

27. (CURRENTLY AMENDED) The polyester-polyethylene multiblock copolymer according to ~~any one of claims 22 to 26~~ claim 22, wherein the dicarboxylic polyethylene is selected from the group consisting of dichloride dicarboxylic (PEG) and dibromide dicarboxylic PEG.

28. (CURRENTLY AMENDED) A method for preparing the polyester-polyethylene multiblock polymer of formula (III) as defined in ~~any one of claims 22 to 27~~ claim 22, comprising the steps of:

a)oxidizing both terminal hydroxyl groups (-OH) of a polyethylene glycol into corresponding carboxylic groups (COOH) by means of a Jones reaction;

b)chlorinating the carboxylic functions of the polyethylene glycol obtained in step a) by making use of a $SOCl_2$ reagent so as to obtain a polyethylene glycol with terminal dichloride acid functions; and

c) reacting the polyethylene glycol having terminal dichloride acid functions obtained in step b) with the PLA-PEG-PLA triblock polymer ~~obtained in claim 34~~ of formula (I):

ABA-(c-ABA)$_n$-c-ABA (I)

wherein

- n is a number equal or higher than 2;
- ABA is a PLA-PEG-PLA triblock; and
- c is a carboxylic diacid; and

said method comprising the steps of:

a) preparing a PLA-PEG-PLA triblock;

b) mixing the PLA-PEG-PLA triblock prepared in step a) with a diacid selected from the group consisting of propanedioic acid, butanedioic acid and pentanedioic acid by making use of polycondensation reaction so as to obtain a multiblock copolymer ~~as claimed in any one of claims 3 to 12~~ comprising a series of polyester and polyethylene blocks which alternate so as to form a repetitive sequence.

29. (ORIGINAL) An improved method for preparing a PLA-PEG-PLA multiblock copolymer of formula (I):

ABA-(c-ABA)$_n$-c-ABA (I)

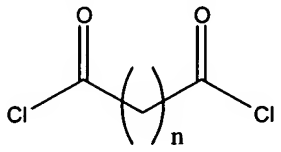
wherein

- n is a number equal or higher than 2;
- ABA is a PLA-PEG-PLA triblock; and
- c is a carboxylic diacid.

said method comprising the steps of:

a) preparing a PLA-PEG-PLA triblock;

b) mixing the PLA-PEG-PLA triblock prepared in step a) with a diacid of formula (II):



(II)

wherein n is a number equal to or greater than 1; and

c) subjecting the mixture of step b) to a polycondensation reaction with the presence of a dicyclohexylcarboxydiimide reagent and/or a chemical equivalent thereof, said catalyst improving the efficiency of the reaction, thereby allowing to obtain the requested multiblock copolymer.

30. (ORIGINAL) The method according to claim 29, wherein step a) comprises the steps of:

(i) reacting at least one monomer A with at least one monomer B by a polycondensation reaction so as to produce a PLA-PEG-PLA triblock;

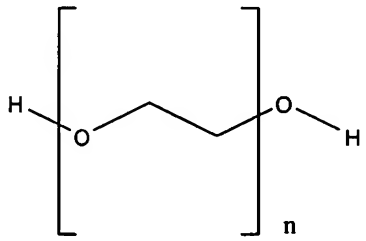
(ii) dissolving the PLA-PEG-PLA triblock obtained in step (i) in acetone;

(iii) precipitating the dissolved PLA-PEG-PLA triblock in step (ii) in water; and

(iv) washing and drying the PLA-PEG-PLA triblock polymer.

31. (ORIGINAL) The method according to claim 30, wherein monomer A is selected from the group comprising of dioxanediones, lactones and dioxanones.

32. (CURRENTLY AMENDED) The method according to claim 30 ~~or 31~~, wherein monomer B is a polyethylene glycol (PEG) represented by the formula (B):



wherein n represents a number between 200 and 2000.

33. (CURRENTLY AMENDED) The method according to ~~any one of claims 30 to 32~~ claim 30, wherein step (ii) is carried out with a tin based catalyst at a temperature between 160° C and 180° C under an inert atmosphere.

34. (CURRENTLY AMENDED) The method according to ~~any one of claims 29 to 33~~ claim 29, wherein the diacid chloride used in step b) is selected from the group comprising of propanedioic acid, butanedioic acid and pentanedioic acid.

35. (CURRENTLY AMENDED) The method according to ~~any one of claims 29 to 34~~ claim 29, wherein the chemical equivalent of dicyclohexylcarboxydiimide (DCC) is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC).

36. (CURRENTLY AMENDED) The method according to ~~any one of claims 29 to 35~~ claim 29, wherein the carboxylic diacid in step c) is selected, the group comprising of butanedioic acid, propanedioic acid and pentanedioic acid.

37. (CURRENTLY AMENDED) A method for delivering a pharmaceutical compound into a mammal, said method comprising the step of: administering to the mammal a stealthy polymeric biodegradable nanosphere as claimed in ~~any one of claims 1 to 20~~ claim 1 loaded with a therapeutically effective amount of the pharmaceutical compound.

38. (ORIGINAL) The method according to claim 37, wherein the pharmaceutical compound comprises a therapeutic agent which is selected from the group of anticancer agents, immunosuppressive agents, agents for steroid therapy, anti-arrhythmic agents, antibiotics, antiparasitics, antivirals, antifungics, gene-therapy agents, antisense molecules, orphan drugs, and vitamins.

39. (CURRENTLY AMENDED) The method according to claim 37 ~~or 38~~, further comprising other agents allowing for a targeted delivery of the pharmaceutical compound into the mammal.

40. (ORIGINAL) The method according to claim 39, wherein the other agent is an antibody.

41. (CURRENTLY AMENDED) Method for preparing stealthy polymeric biodegradable nanospheres from an emulsion, the method comprising the step of:

(i) prepraring an organic internal phase comprising a pharmaceutical compound, a polyester-polyethylene multiblock as defined in ~~any one of claims 3 to 12~~ claim 3 and/or a blend of polymers and a polyester;

(ii) preparing an aqueous external phase;

(iii) injecting both the organic internal phase of step (i) and the aqueous external phase of step (ii) into a homogenization chamber having an outlet, with or without a surfactant, thereby producing an emulsion at the outlet of the chamber;

(iv) evaporating and/or extracting the phases of step (iii) so as to produce stealthy polymeric nanospheres; and

(v) collecting the stealthy polymerice nanospheres obtained in step (iv) by centrifugation or dialysis.

42. (ORIGINAL) Method according to claim 41, wherein a primary emulsion is used instead of the organic phase of step (i) when the pharmaceutical compound a hydrophilic drug.

43. (ORIGINAL) Method according to claim 42, wherein the primary emulsion is obtained by dispersing an aqueous solution into an organic solution containing polymers.

44. (CURRENTLY AMENDED) Method according to ~~any one of claim 41 to 43~~ claim 41, wherein the blend of polymers is a multiblock polymer mixed with a polyester selected from the group comprised of PLA, PCL and PLGA.